EXHIBIT R

PROLENE® MESH

Polypropylene

Technical File

Strictly Confidential Document

July 1995

ETHNOR S.A. **ETHICON FRANCE**

SUMMARY

SECTION

II. CONFORMITY WITH ESSENTIAL REQUIREMENTS

II.1. GENERAL REQUIREMENTS

1. "The devices are to be designed and manufactured in such a way that their use does not compromise the clinical state and the safety of the patients nor the safety and health of the users or, where applicable, of other persons, when they are used under the conditions and for the purposes anticipated, it being understood that the possible risks linked to their use constitute risks that are acceptable with regard to the benefit brought to the patient and are compatible with a high level of protection of health and safety."

The PROLENE® Mesh manufactured by Ethnor SA is inspected in conformity with the requirements of the quality system ISO 9001/EN 29001 and NF EN 46001 applied according to the NF EN 724 guide.

⇒ ISO 9001 - Quality systems - Model for quality assurance in design/development, production, installation and servicing after sale.

⇒ NF EN 46001 - Quality systems - Medical devices - Specific requirements related to the application of EN 29001.

⇒ NF EN 724 - Guide for application of EN 29001 and EN 46001 and of EN 29002 and EN 46002 for non-active medical devices.

The publications relative to the clinical use of PROLENE® Mesh are added in Section VI.

2. "The solutions chosen by the manufacturer in the design and construction of the devices must be in accordance with the principles of integration of safety, taking into account the generally recognized state of the art."

The safety principles used in the original design and the construction of the device were those required by the FDA when it was first developed in the United States. The manufacture by Ethnor SA was originally in conformity with the requirements of the Guide to good manufacturing practices for sterile medical materials and surgical products. It is now in conformity with EN 29001 and EN 46001 as specified in 1, above.

3. "The devices must attain the performances assigned to them by the manufacturer and should be designed, manufactured and packaged so as to be capable of fulfilling one or several of the functions referred to in Article 1, paragraph 2, point a) and such as are specified by the manufacturer."

PROLENE® Mesh can be used in humans and conforms to the definition of a medical device as in paragraph 2, point a) of the first Article of the EEC Directive 93/42. The performances assigned by the manufacturer are shown in the instructions for use. The indications, contraindications, warnings and precautions for use are also recorded.

4. "The characteristics and performances referred to in points 1, 2 and 3 must not be changed in such a way as to compromise the clinical state and the safety of the patients and, where applicable, other persons for the duration of the life of the devices following the indications of the manufacturer when these devices are subjected to the stresses that can arise under normal conditions of use."

PROLENE® Mesh is a single-use device. The life of the product is equivalent to the duration of its implantation in the organism. The studies reported in Section VII show that PROLENE® Mesh is well tolerated in the organism.

5. "The devices must be designed, manufactured and packaged in such a way that their characteristics and their performances in view of their intended use are not changed during storage and transportation, bearing in mind the instructions and information provided by the manufacturer."

The storage time for PROLENE® Mesh is five years if the device is stored at a temperature below 25 degrees Celsius, away from humidity and direct heat. Stability studies show that the characteristics and performances are unchanged under these conditions until it is used. The shelf life of the device is shown on the wrapping. The instructions for use state that the device is not to be used after the expiration date.

6. "Any secondary, undesirable effect must constitute an acceptable risk with respect to the performances ascribed."

When PROLENE® Mesh is used, a slight inflammatory reaction can be observed. This is due in part to the natural healing process.

Warnings and precautions for use of the device are specified in the instructions for use.

II.2. REQUIREMENTS RELATED TO DESIGN AND CONSTRUCTION

7. Chemical, physical and biological properties.

7.1. The devices must be designed and manufactured so as to assure the characteristics and performances referred to in Section 1 "General requirements." Particular attention must be paid to:

- **the choice of materials used, especially as far as toxicity and, if applicable, the flammability are concerned.**

- **the mutual compatibility of the materials used, the tissues and biological cells, and also the body fluids, taking into account the intended use of the device.**

PROLENE® Mesh is composed of non-absorbable filaments of polypropylene, the composition of which is identical to that of PROLENE® suture threads. The biocompatibility studies presented are therefore those carried out on PROLENE® sutures.

PROLENE® Mesh has been used since 1973. The bibliographical references relating to PROLENE® in the mesh form give a selection of various surgical uses of this device and demonstrate that it can be used in complete safety.

⇒ In vitro cytotoxicity

- Report of ETHICON Limited Study No. 39/93, 04/30/93: no cytotoxicity was demonstrated.
- PTS accession No. 92-1411: no toxic effect was demonstrated.

⇒ In Vivo cytotoxicity

- Biological evaluation of PROLENE® Mesh: ERF Accession No. 73-130. After a 3-day implantation, a minor edematous reaction is observed with minimal proliferation of fibroblasts. The proliferation of collagen fibers is classically observed after 28 days of implantation. A minor foreign body reaction is noted.
- Study of tissue reactions to polypropylene thread (PROLENE®): Report of ETHICON Limited Study No. 38/82, 09/27/82.
  The tissue reactions observed between day 1 and day 120 are very minor and are confirmed long-term.
- Report of ETHICON Limited Study, 10/14/65: ocular implantation of PROLENE® suture in the rabbit.
  The polypropylene thread maintained its properties to term and appeared to be inert.

⇒ Carcinogenicity

- Report of ETHICON Limited Study 10/14/65: observation after a 3-month implantation in the dog and a 24-month implantation in the rat.
  No carcinogenic effect was demonstrated.

(COPIES OF STUDIES: see Section VI)

7.2. The devices must be designed, manufactured and packaged so as to minimize the risk presented by contaminants and residues for personnel involved in transportation, storage and use as well as for the patients, in conformity with the intended use of the product. Particular attention must be paid to the tissues exposed, as well as to the duration and frequency of exposure.

PROLENE® Mesh is sterilized with ethylene oxide. The amount of ethylene oxide residues resulting from the sterilization cycle has been determined and is substantially lower (< 1 ppm) than the amount considered acceptable in the norm ISO/DIS 10993-7, "Biological evaluation of medical devices - Residues from sterilization with ethylene oxide."

7.3. The devices must be designed and manufactured so that they can be used in complete safety with the materials, substances and gases with which they enter into contact in the course of their normal use or during routine procedures; if the devices are intended for the administration of medications, they must be designed and manufactured so as to be compatible with the medications involved, in conformity with the provisions and restrictions applicable to the latter, and so that their performance is maintained in conformity with their intended use.

No publication to date has mentioned problems associated with interactions between PROLENE® Mesh and other materials, substances or gases. Under normal conditions of use, PROLENE® Mesh thus does not present this type of interaction risk.

7.4. When a device incorporates as an integral part a substance which, if used separately, may be considered a medication as defined by Article 1 of the Directive 65/65/EEC, and which can act on the human body by an action secondary to that of the device, the quality and usefulness of this substance must be verified, taking into consideration the intended use of the device, by analogy with the appropriate methods contained in the Directive 75/318/EEC.

Not applicable.

7.5. The devices must be designed and manufactured so as to reduce to a minimum the risks arising from substances escaping from the device.

Not applicable.

7.6. The devices must be designed and manufactured so as to minimize as much as possible the risks due to unintentional passage of substances into the device, taking into account the device and the nature of the environment in which it is designed to be used.

Not applicable.

8. Infection and microbial contamination

8.1. "The devices and their manufacturing processes must be designed in such a way as to eliminate or reduce as much as possible the risk of infection for the patient, the user and third parties. The design must allow easy handling and, as far as necessary, minimize the contamination of the device by the patient or vice versa in the course of use."

The risk of infection for the patient is eliminated by the following means:

⇒ The manufacture is carried out in a monitored and periodically checked environment.

⇒ The initial contamination of the product is measured in order to check the quality of the manufacturing environment.

⇒ The product is sterilized with ethylene oxide. [orig. erroneously states "...sterilized by irradiation."]

Checking of the environment

The microbial contamination of work sites and the atmosphere is regularly monitored. Corrective measures are undertaken if the results are higher than the predetermined values.

Checking of initial contamination of the product

The bioburden is measured regularly on samples taken at random immediately before sterilization.

Sterilization of the product

The product is sterilized with ethylene oxide [orig. erroneously states "... sterilized by irradiation."] according to a procedure validated and checked in conformity with EN 550 "Sterilization of medical devices. Method of validation and routine checking of sterilization with ethylene oxide." The sterility assurance level is 10^{-6} and the product is labelled "Sterile" in conformity with the requirements of EN 556 "Sterilization of medical devices. Requirements for medical devices labelled Sterile."

8.2. "Tissues of animal origin must come from animals that have been subjected to veterinary inspections and monitoring measures adapted to the use for which the tissues are intended."

Not applicable.

8.3. "Devices which are supplied in the sterile state must be designed, manufactured and packaged in non-reusable packaging and/or according to appropriate procedures so that they are sterile at the time they are put on the market and that under the conditions for storage and transportation laid down they maintain this quality until the protective packaging assuring sterilization is damaged or opened."

The following measures contribute to the assurance of the fulfillment of the above requirements.

8.3.1. Validation and type of wrapping.

The product is packaged in a non-reusable, heat-sealed wrapping composed of a blister closed with a sheet of Tyvek®.

Validation includes the evaluation of the following properties:

⇒ Compatibility of packaging and product

⇒ The compatibility of the packaging and the sterilization procedure. This point is included in the validation of the sterilization process.

⇒ The microbiological barrier properties of the packaging

⇒ The integrity of the seal.

The various materials used have been demonstrated to be in conformity with the preceding requirements.

8.3.2. Stability data and storage recommendations

Various studies have been carried out at ambient temperature (not controlled) and for a period of five years to make sure of the stability of the product and of its packaging. No deterioration of the packaging was observed and the product remained sterile and retained its physical properties, which proves the effectiveness of the packaging materials and of the sealing process. The storage conditions recommended as a result of these studies are: storage below 25 degrees C, away from humidity and heat. The shelf life is five years. The storage conditions are shown in the instructions for use. The expiration date is indicated on each package and on each box.

8.4. "Devices which are supplied in the sterile state must have been manufactured and sterilized by an appropriate, validated method."

8.4.1. Sterilization procedures

PROLENE® Mesh is sterilized with ethylene oxide - see Section IV.

8.4.2. Validation procedures

Validations of the ethylene oxide sterilization procedure were carried out according to ETHNOR SA internal procedures, applying procedures of Johnson & Johnson.

Future validations will be carried out in conformity with the requirements of EN 550 "Sterilization of medical devices. Validation and routine control of sterilization with ethylene oxide." See Section IV.4.2.

8.5. "Devices that are intended for sterilization must be manufactured under conditions satisfying the appropriate controls (for example, environmental control)."

Not applicable. The devices manufactured by ETHNOR are offered in the sterile state.

8.6. "Systems of packaging intended for non-sterile devices must be such as to preserve the product without deterioration at the level of cleanliness provided for and, if they are intended to be sterilized before their use, to minimize the risk of microbial contamination."

Not applicable. The devices manufactured by ETHNOR are offered in the sterile state.

9. Properties relating to manufacture and the environment

9.1. The precautions and warnings relating to the use of PROLENE® Mesh are given in the instructions for use.

9.2. PROLENE® Mesh is offered in several sizes. The choice of the most appropriate size falls to the surgeon.

Polypropylene is a material that must not be used in direct contact with a heat source that could cause melting.

Aging studies and stability studies carried out before product market availability indicated that risks arising from the aging of the materials are not a factor. The expiration period of these devices is set at 5 years. The expiration date is inscribed on each package box and on each wrapping.

10. Devices with a measurement function.

Not applicable.

11. Protection against radiation.

Not applicable.

12. Requirements for medical devices connected to an energy source or equipped with such a source.

Not applicable.

13. Information provided by the manufacturer.

13.1. "Each device must be accompanied by the information required for it to be able to be used in complete safety and to permit identification of the manufacturer, taking into account the training and knowledge of the potential users.

This information comprises the indications in the instructions for use.

To the extent possible and appropriate, the information required for the use of the device in complete safety must be on the device itself and/or on the wrapping of each unit or, where appropriate, on the commercial wrapping. If it is not possible to wrap each unit separately, the information must be on a sheet accompanying one or more devices.

The packaging of each device must contain instructions for use. An exception is made for devices of classes I and IIa, if they can be used completely safely without the aid of such instructions."

The labelling of the primary wrapping or of the box is in conformity with the requirements of the European Standards on Labelling prEN 1041 "Information provided by the manufacturer with medical devices." They correspond to Sections 13.1 to 13.5 of Appendix I of the Directive relating to medical devices. The symbols used are in conformity with prEN 980 "Graphic symbols used in the labelling of medical devices." The key to these symbols is repeated in the instructions for use.

PROLENE® Mesh is a Class IIb device in conformity with Rule 8 of Appendix IX. Instructions for use are included in each unit intended for sale. The instructions are reproduced in Section IX and are in conformity with the requirements of the European Standards on Labelling and with Section 13.6 of Appendix I when appropriate.

VI. BIOLOGICAL STUDIES

VI.1. CYTOTOXICITY STUDIES

- Report of study by ETHICON Limited, No. 39/93
- PTS ACCESSION No. 92-1411 of 1/25/93, attached
- ERF Accession No. 73-130
- Report of study by ETHICON Limited, No. 38-82
- Report of study by ETHICON Limited, 10/14/65.

06003

(Ethicon Limited Report No. 39/93, 30.4.93)

Summary

Samples of metric 1.0 sutures were examined for in-vitro cytotoxicity using the Agar overlay and Extraction/Neutral Red Uptake tests.

Sample Preparation	- Sutures were cut to 1 cm lengths for the Agar Overlay Test. Extracts were prepared in serum containing growth medium for 24 hours at 37 deg C for the Neutral Red Uptake test. Extract strength was 1.0 cm^2/ml.
Cell Line	- NCTC Clone L929 Mouse Fibroblasts Passage No. 608-610.
Medium	- Minimum Essential Medium (MEM) with Earle's Salts, 5% foetal calf serum, 1 mm glutamine, 1% non-essential amino acids, 2.2 g/litre $NaHCO_3$.
Procedure Agar Overlay	- Samples were added directly to the cell monolayers in the Agar Overlay system.
Results Agar Overlay	- No zone of cytotoxicity was found. Cells were stained and intact.
Procedure Neutral Red Uptake	- Extracts and dilutions (50%) were exposed to cells for 24 hours in 96 well microplates. Optical density was read at 540 nm on a microplate reader.
Results Neutral Red Uptake	- Little or no reduction in Neutral Red Uptake.

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ETHICON, Inc.
a Johnson & Johnson company
Department of
Pathology, Toxicology & Surgery

06004

JAN 25 1993

K. Purcell (Cornelia)

cc: S. H. Liu
RDCF

IN VITRO CYTOTOXICITY:
PROLENE POLYPROPYLENE MESH:
LOT #D356 2980 - NORMAL PRODUCTION,
SCOURED AND W/ETHASEW WAX AS A LUBRICANT;
LOT #D42990 - NOT SCOURED AND
W/PARAFFIN OIL AS A LUBRICANT;
LOT #D2949 - SCOURED AND
W/PARAFFIN OIL AS A LUBRICANT

PTS ACCESSION NO.

92-1411

PROJECT NO. 99999

The above-captioned samples, and extracts thereof, were non-cytotoxic when tested in the agar overlay assay. The results of these studies are summarized in the attached copies of the final reports issued by North American Science Associates, Inc. on January 7, 1993.

Lisa Martini 1/25/93
L. Martini, B.S.
Study Coordinator
Associate Scientist, Toxicology

J. F. Dooley 1/25/93
J. F. Dooley, Ph.D.
Principal Scientist, Toxicology

Attachment
G:\92-1411R.LMH

ETHICON INC.
JAN 2 0 1993
RD-CENTRAL FILE

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ATTN: LISA MARTINI

06005

CYTOTOXICITY - AGAROSE OVERLAY

Test Article: Prolene polypropylene mesh Lot #D356 2980; Normal Production, scoured and with Ethasew Wax

Test Article Description: Mesh - 1 sq. cm piece

Procedure: A monolayer of L-929 mouse fibroblast cells was grown to confluency and overlaid with Minimum Essential Medium supplemented with serum, antibiotics, neutral red, and agarose. The test article, a 0.5 cm x 0.5 cm piece of P-11102 as a positive control, and a 1.0 cm length piece of USP negative control were placed on the solidified overlay surface. Following incubation for 24 hours, the culture was macroscopically examined for evidence of cell decolorization to determine the zone of cell lysis. Any decolorized zone present was examined microscopically to confirm cell lysis.

Score	Observations
N (Nontoxic)	No change in cell morphology in proximity to test sample.
T (Toxic)	Death and/or degeneration of cells directly beneath the area of test sample and possibly also within a zone extended beyond the test sample. Where a zone of lysis was observed, the distance from the edge of the sample to the edge of the zone was measured and reported in millimeters (mm).

Results:

Test/Control Articles	Score	Zone of Lysis (mm)
Test Article Results	N	0
USP Negative Control	N	0
Positive Control: P-11102	T	9

Conclusion: The above test article was nontoxic for L-929 mouse fibroblast cells under the above described test parameters.

Comments: Not Applicable.
Date Prepared: 1-5-93 Date Terminated: 1-6-93

Ims Completed 1-7-93 Tech. LMN/JMT Approved [signature]

MG030-110

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LOT NO. 92-1411

ATTN: LISA MARTINI

06006

CYTOTOXICITY - AGAROSE OVERLAY WITH EXTRACTION

Test Article: Prolene polypropylene mesh Lot #D356 2980; Normal Production, scoured and with Ethasew Wax

Procedure: The test article was prepared by extracting 60 sq. cm in 20 ml of 0.9% SC in an extraction vessel at 37°C for 24 hour(s). A monolayer of L-929 mouse fibroblast cells was grown to confluency and overlaid with Minimum Essential Medium supplemented with serum, antibiotics, neutral red, and agarose. A 0.1 ml portion of the test article extract on a filter paper disc was placed on the solidified overlay surface. Also placed on the agarose surface was: (a) a filter paper disc saturated with 0.1 ml 0.9% SC as a negative control, (b) a 1.0 cm length piece of USP negative control, and (c) a 0.5 cm x 0.5 cm piece of P-11102 as a positive control. Following incubation for 24 hours, the culture was macroscopically examined for evidence of cell decolorization to determine the zone of cell lysis. Any decolorized zone present was examined microscopically to confirm cell degeneration or lysis.

Score	Observations
N (Nontoxic)	No change in cell morphology in proximity to test article.
T (Toxic)	Death and/or degeneration of cells directly beneath the area of test sample and possibly also within a zone extended beyond the test sample. Where a zone of lysis was observed, the distance from the edge of the sample to the edge of the zone was measured and reported in millimeters (mm).

Results:

Test/Control Articles	Score	Zone of Lysis (mm)
Test Article Results	N	0
USP Negative Control	N	0
Filter Disc Control: 0.9% SC	N	0
Positive Control: P-11102	T	8

Conclusion: The above test article was nontoxic for L-929 mouse fibroblast cells under the above described test parameters.

Comments: Not Applicable.
Date Prepared: 1-4-93 Date Terminated: 1-6-93

lms Completed 1-7-93 Tech. KSH/SDR/LMN Approved James M. Bruce
MMA

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LOT NO. 92-1411

ATTN: LISA MARTINI

06007

CYTOTOXICITY - AGAROSE OVERLAY

Test Article: Prolene polypropylene mesh Lot #D42990, not scoured, with Parafin oil as lubricant

Test Article Description: Mesh - 1 sq. cm piece

Procedure: A monolayer of L-929 mouse fibroblast cells was grown to confluency and overlaid with Minimum Essential Medium supplemented with serum, antibiotics, neutral red, and agarose. The test article, a 0.5 cm x 0.5 cm piece of P-11102 as a positive control, and a 1.0 cm length piece of USP negative control were placed on the solidified overlay surface. Following incubation for 24 hours, the culture was macroscopically examined for evidence of cell decolorization to determine the zone of cell lysis. Any decolorized zone present was examined microscopically to confirm cell lysis.

Score	Observations
N (Nontoxic)	No change in cell morphology in proximity to test sample.
T (Toxic)	Death and/or degeneration of cells directly beneath the area of test sample and possibly also within a zone extended beyond the test sample. Where a zone of lysis was observed, the distance from the edge of the sample to the edge of the zone was measured and reported in millimeters (mm).

Results:

Test/Control Articles	Score	Zone of Lysis (mm)
Test Article Results	N	0
USP Negative Control	N	0
Positive Control: P-11102	T	9

Conclusion: The above test article was nontoxic for L-929 mouse fibroblast cells under the above described test parameters.

Comments: Not Applicable.
Date Prepared: 1-5-93 Date Terminated: 1-6-93

lms Completed 1-7-93 Tech. LMN/JMT Approved

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LOT NO. 92-1411

ATTN: LISA MARTINI

06008

CYTOTOXICITY - AGAROSE OVERLAY WITH EXTRACTION

Test Article: Prolene polypropylene mesh Lot #D42990, not scoured, with Parafin oil as lubricant

Procedure: The test article was prepared by extracting 60 sq. cm in 20 ml of 0.9% SC in an extraction vessel at 37°C for 24 hour(s). A monolayer of L-929 mouse fibroblast cells was grown to confluency and overlaid with Minimum Essential Medium supplemented with serum, antibiotics, neutral red, and agarose. A 0.1 ml portion of the test article extract on a filter paper disc was placed on the solidified overlay surface. Also placed on the agarose surface was: (a) a filter paper disc saturated with 0.1 ml 0.9% SC as a negative control, (b) a 1.0 cm length piece of USP negative control, and (c) a 0.5 cm x 0.5 cm piece of P-11102 as a positive control. Following incubation for 24 hours, the culture was macroscopically examined for evidence of cell decolorization to determine the zone of cell lysis. Any decolorized zone present was examined microscopically to confirm cell degeneration or lysis.

Score	Observations
N (Nontoxic)	No change in cell morphology in proximity to test article.
T (Toxic)	Death and/or degeneration of cells directly beneath the area of test sample and possibly also within a zone extended beyond the test sample. Where a zone of lysis was observed, the distance from the edge of the sample to the edge of the zone was measured and reported in millimeters (mm).

Results:

Test/Control Articles	Score	Zone of Lysis (mm)
Test Article Results	N	0
USP Negative Control	N	0
Filter Disc Control: 0.9% SC	N	0
Positive Control: P-11102	T	8

Conclusion: The above test article was nontoxic for L-929 mouse fibroblast cells under the above described test parameters.

Comments: Not Applicable.
Date Prepared: 1-4-93 Date Terminated: 1-6-93

lms MMcl Completed 1-7-93 Tech. KSH/SDR/LMN Approved

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LOT NO. 92-1411

06009

ATTN: LISA MARTINI

CYTOTOXICITY - AGAROSE OVERLAY WITH EXTRACTION

Test Article: Prolene polypropylene mesh, Lot #D2949; scoured & with Parafin oil as lubricant

Procedure: The test article was prepared by extracting 60 sq. cm in 20 ml of 0.9% SC in an extraction vessel at 37°C for 24 hour(s). A monolayer of L-929 mouse fibroblast cells was grown to confluency and overlaid with Minimum Essential Medium supplemented with serum, antibiotics, neutral red, and agarose. A 0.1 ml portion of the test article extract on a filter paper disc was placed on the solidified overlay surface. Also placed on the agarose surface was: (a) a filter paper disc saturated with 0.1 ml 0.9% SC as a negative control, (b) a 1.0 cm length piece of USP negative control, and (c) a 0.5 cm x 0.5 cm piece of P-11102 as a positive control. Following incubation for 24 hours, the culture was macroscopically examined for evidence of cell decolorization to determine the zone of cell lysis. Any decolorized zone present was examined microscopically to confirm cell degeneration or lysis.

Score	Observations
N (Nontoxic)	No change in cell morphology in proximity to test article.
T (Toxic)	Death and/or degeneration of cells directly beneath the area of test sample and possibly also within a zone extended beyond the test sample. Where a zone of lysis was observed, the distance from the edge of the sample to the edge of the zone was measured and reported in millimeters (mm).

Results:

Test/Control Articles	Score	Zone of Lysis (mm)
Test Article Results	N	0
USP Negative Control	N	0
Filter Disc Control: 0.9% SC	N	0
Positive Control: P-11102	T	10

Conclusion: The above test article was nontoxic for L-929 mouse fibroblast cells under the above described test parameters.

Comments: Not Applicable.
Date Prepared: 1-4-93 Date Terminated: 1-6-93

lms Completed 1-7-93 Tech. KSH/SDR/LMN Approved

MG030-130

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LOT NO. 92-1411

ATTN: LISA MARTINI

06010

CYTOTOXICITY - AGAROSE OVERLAY

Test Article: Prolene polypropylene mesh, Lot #D2949; scoured & with Parafin oil as lubricant

Test Article Description: Mesh - 1 sq. cm piece

Procedure: A monolayer of L-929 mouse fibroblast cells was grown to confluency and overlaid with Minimum Essential Medium supplemented with serum, antibiotics, neutral red, and agarose. The test article, a 0.5 cm x 0.5 cm piece of P-11102 as a positive control, and a 1.0 cm length piece of USP negative control were placed on the solidified overlay surface. Following incubation for 24 hours, the culture was macroscopically examined for evidence of cell decolorization to determine the zone of cell lysis. Any decolorized zone present was examined microscopically to confirm cell lysis.

Score	Observations
N (Nontoxic)	No change in cell morphology in proximity to test sample.
T (Toxic)	Death and/or degeneration of cells directly beneath the area of test sample and possibly also within a zone extended beyond the test sample. Where a zone of lysis was observed, the distance from the edge of the sample to the edge of the zone was measured and reported in millimeters (mm).

Results:

Test/Control Articles	Score	Zone of Lysis (mm)
Test Article Results	N	0
USP Negative Control	N	0
Positive Control: P-11102	T	8

Conclusion: The above test article was nontoxic for L-929 mouse fibroblast cells under the above described test parameters.

Comments: Not Applicable.
Date Prepared: 1-5-93 Date Terminated: 1-6-93

lms MNM Completed 1-7-93 Tech. LMN/JMT Approved Marie M Bruch

MG030-110

06011

PLEASE USE YELLOW HIGHLIGHTER PEN TO HIGHLIGHT WORDS

ERF Acc. No. 92-1411

1) ADDITIONAL SAMPLE DESCRIPTION
(include only if not in title)

Form:

Mesh	Mono
Staple	Braid
Clip	Dyed
Absorbable	Undyed
Adhesive	Coating_____
Film	Size_____
Coupler	Other_____
Non-absorbable	

2) ADDITIONAL STUDY DESCRIPTION

Study Type:

Tissue reaction	Demonstration
orption	Sales School
eaking strength	Laser
Function	GLP
Developmental	Ex vivo
Product Service Review	In vitro
Product Inquiry Affiliate	Dept. objective
Veterinary inquiry	Training study
Pilot	Competitive test
Cancer	Comparative
Allergen	Patency
Intracutcut Irritat	Stability
Mutagen	Hinge strength
Pyrogen	Tensiometry
Acute tox	Photomicrography
Gross TR	
Other CYTOTOXICITY	

plant Site:

	Stomach
IM	Genital tract
Eye	Lung
Vascular	Skin
IP	Small intestine
IV	Spleen
Intradermal	Colon
Dura	Bone
Urinary bladder	Other_____

Implant period-days: List

Test system:

Rat	Cell culture
Mouse	Guinea pig
Rabbit	Pig
Dog	Goat
Human	Other_____

Photography:

Gross photo	Video
Micro photo	SEM photo
TEM photo	Other_____

3) ADDITIONAL HISTOLOGY DESCRIPTION:

Embed:

GMA	Ground section
Frozen section	Other_____

Special Stains:

ORO	Iron
Silver	Calcium
Trichrome	Geimsa
PAS	Gram
PTAH	Immunohistochem
VG	Other_____

Slides, no slides, histopath report

4) SURGICAL DESCRIPTION:

Anastomosis vascular	Keratotomy
Anastomosis-_____	Laparotomy
Colotomy	Lobectomy
Craniotomy	Splenectomy
Cystotomy	Thoracotomy
Gastrotomy	Ligation
Ovariohysterectomy	Other_____

5) MISCELLANEOUS:

Biochem analysis	Other_____
Clinical pathology	Other_____
Radiography	Other_____
Biomechanics test	

633A/cal

TECHNICAL REPORT

ETHICON
RESEARCH
FOUNDATION
SOMERVILLE, NEW JERSEY

73-2675

06012

August 21, 1973

To: Mr. E. A. Block

cc: Dr. C. Artandi
Dr. P. V. Buday
Dr. J. P. Jones
Dr. R. L. Kroner
Mr. T. N. Salth
RDCF

Subject: PROLENE* MESH - BIOLOGICAL EVALUATION IN RABBITS (3, 28 days)

ERF ACCESSION NO.

73-130

Project No. 20901

SUMMARY

PROLENE* mesh was implanted subcutaneously in the abdominal wall of twelve albino rabbits for 3 and 28 days to determine its tissue response.

A minimal to slight acute response consisting of transient edema, hemorrhage or hyperemia, and inflammatory cell infiltration was elicited by PROLENE mesh. This reaction was supplanted by moderate fibrous encapsulation of mesh filaments and connective tissue formation in spaces between filaments after one month of implantation.

The reactions to PROLENE mesh were similar in type and extent to the response elicited by Marlex mesh implanted as a control.

ETHICON, INC.

AUG 27 1973

RD-Central File

Reported By M. H. Wykoff / A. Abdelleyue
Dr. M. H. Wykoff
Dr. J. A. Williams

Approved By P. H. Craig JAR
Dr. Peter H. Craig

rb

*Tradem

Materials:

ERF No.	Lot	Description	Sterility No.**
1	1131-110-3	PROLENE* mesh 5 cm x 2 cm	F158KB1
2	1131-110-2	Marlex mesh 5 cm x 2 cm	F158KB1

** Ethylene oxide sterilized.

Procedures:

Six male and six female albino rabbits were anesthetized and shaved from the xiphoid cartilage to the pubis. The skin was incised bilaterally 2 cm from the midline at the level of the umbilicus. The skin was then separated from the subcutaneous fascia so that a pocket was formed to accept a mesh sample. A sample of either PROLENE or Marlex mesh 2 x 5 cm was then inserted into this pocket and the skin closed with ETHILON* sutures. Both Marlex and PROLENE meshes were placed an equal number of times on the left and right sides of rabbits of each sex.

At necropsy implant sites were examined for gross lesions. The implant along with overlying skin and underlying abdominal muscle was removed and fixed in buffered formalin for histologic preparation. From each site, two sections stained with hematoxylin and eosin were prepared and examined for inflammatory response and connective tissue proliferation in implants.

Results:

Gross Observations at Necropsy:

No untoward abnormality was noted at necropsy for either the PROLENE mesh or Marlex mesh implanted as a control. Minimal hemorrhage was noted in three PROLENE mesh and two Marlex mesh sites after three days. Minimal or slight edema was observed in three implant sites for each material. No observable gross changes were found for either mesh material at 28 days post implantation.

Histopathologic Observations:

Tissue response to PROLENE mesh implanted subcutaneously in the abdominal wall of rabbits was graded minimal or slight at 3 and 28 days post implantation in all but two sites. The responses elicited by PROLENE mesh were similar in type and extent to

Marlex mesh implanted as a control. Details of responses in individual animals are set forth in Tables 1-4.

At 3 days post implantation minimal erythrocyte extravasation, mild edema, slight vascular proliferation, scattered macrophages and a few heterophils were typical of responses present around PROLENE* mesh implants. Proliferation of fibroblasts was minimal at this interval. Some difficulty was encountered in retaining morphologic relationship of implant to adjacent tissues at the early interval.

Collagenous fiber proliferation around PROLENE mesh filaments typified the response noted at 28 days post implantation. Collagenous fibers also extended between filaments filling in mesh spaces. A mild foreign body giant cell reaction was noted, but was not different from that seen associated with Marlex implants. Neither was fibrous tissue proliferation around Marlex implants more extensive than noted around PROLENE mesh implants.

Pyogenic response in two implant sites, Marlex rabbit #1 at 3 days and PROLENE mesh rabbit #5 at 28 days were noted. These responses were believed to be related to inadvertent infection associated with surgical implantation and not due to reaction to the implanted mesh materials.

*Trademark

Table 1

TISSUE RESPONSE TO PROLENE* MESH
3 DAYS POST IMPLANTATION SUBCUTANEOUSLY IN RABBITS

al	Rabbit No.	Sex	Site	Overall Response	Comments on Response
Mesh 0-3	1	M	Left	Slight	Two sections examined. Slight hemorrhage and edema peripheral to implant. Minimal heterophil infiltration was noted around 10-20% of fibers. Early granulation tissue around implant fibers.
	2	M	Right	Minimal	Two sections examined - minimal granulation tissue formation; delicate connective tissue and vascular proliferation around implanted fibers the only reaction noted.
	3	M	Left	Minimal	Details same as 2R.
	7	F	Left	Slight	Two sections examined. Implant was folded in site. Details of response similar to #1 left.
	8	F	Right	Slight	Two sections examined. Implant folded in site. Slight sero-fibrinous exudate, slight hyperemia and extravasation of erythrocytes noted around mesh fibers. Occasional focus of heterophils around fibers was noted.
	9	F	Left	Minimal	Two sections examined. Minimal inflammatory response noted. A few macrophages around some implant fibers were seen. Early fibroblast proliferation in spaces was seen.

Table 2

TISSUE RESPONSE TO MARLEX MESH
3 DAYS POST IMPLANTATION SUBCUTANEOUSLY IN RABBITS

al	Rabbit No.	Sex	Site	Overall Response	Comments on Response
esh)-2	1	M	Right	Moderate	Two sections examined. Moderate diffuse heterophil infiltration in area of implant also slight congestion and hemorrhage along with minimal edema. Pronounced macrophage infiltration adjacent to about half of filaments in sections.
	2	M	Left	Minimal	Two sections examined. Separation of adjacent tissues made assessment difficult. Minimal hyperemia and edema around filaments. A few macrophages were seen around about 10 percent of filaments. Areolar-like connective tissue noted between filaments.
	3	M	Right	Minimal	Two sections examined. Response same as for #2 left.
	7	F	Right	Slight	Two sections examined. Implant was folded. Slight edema, slight hyperemia and minimal hemorrhage were seen around mesh fibers. Minimal heterophils and macrophages in implant sites were noted.
	8	F	Left	Slight	Two sections examined. Response same as for #7 right.
	9	F	Right	Minimal	Two sections examined. Response same as for #2 left.

Table 3

TISSUE RESPONSE TO PROLENE* MESH
28 DAYS POST IMPLANTATION SUBCUTANEOUSLY IN RABBITS

	Rabbit No.	Sex	Site	Overall Response	Comments on Response
sh 3	4	M	Right	Slight	Moderate fibroblastic cell proliferation along with slight vascular proliferation around filaments and in spaces between filaments. Occasional giant cell and a few macrophages adjacent to some filaments; two sections examined.
	5	M	Left	Moderate	In one section a granulomatous reaction surrounding a pyogenic focus of heterophils adjacent to mesh filaments was seen. In the second section a moderate granulation tissue reaction similar to that noted for #4R without suppurative response was seen.
	6	M	Right	Slight	Two sections examined. Response as in #4 right.
	10	F	Right	Slight	Two sections examined. Response primarily fibroblastic proliferation around mesh fibers and filling in spaces. Minimal vascular proliferation. Occasional giant cells, macrophages, and eosinophils seen around filaments. Implant was partially folded over.
	11	F	Left	Slight	Two sections examined. Moderately dense fibrous tissue around filaments and in mesh spaces. Slight foreign body response with scattered giant cells and macrophages around some filaments.
	12	F	Right	Minimal	Two sections examined. Implant was folded. Primary characteristics were moderate proliferation of blood vessels and fibroblasts around fibers and in mesh spaces. Scattered giant cells, macrophages and lymphocytes noted around fibers.

Table 4

TISSUE RESPONSE MARLEX MESH
28 DAYS POST IMPLANTATION SUBCUTANEOUSLY IN RABBITS

ıl	Rabbit No.	Sex	Site	Overall Response	Comments on Response
ːsh)-2	4	M	Left	Slight	Two sections examined. Implant folded. Primary response was proliferation of loose fibrous tissue around filaments and in mesh spaces. Slight foreign body giant cell reaction noted.
	5	M	Right	Slight	Two sections examined. Primary response was moderately dense fibrous tissue proliferation around mesh filament and filling mesh spaces. One to several foreign body giant cells seen adjacent to about 50 percent of filaments.
	6	M	Left	Slight	Two sections examined. Details of response same as #5 right.
	10	F	Left	Minimal	Implant in one section only. Slight connective tissue proliferation among mesh filaments. Minimal foreign body giant cell formation noted.
	11	F	Right	Slight	Implant in one section only. Details of response same as #5 right.
	12	F	Left	Slight	Two sections examined. Skin was absent; had been reflected from site for gross photograph at necropsy. Slight connective tissue proliferation around filaments. Slight foreign body giant cell formation around 50-60 percent of filaments.

06018

Tissue Reaction and Tensile Strength of PROLENE Polypropylene Suture In-Vivo

(Ethicon Limited Report No. 38/82, 27.9.82)

06019

Summary

Blue dyed PROLENE sutures, gauge sizes metric 1.0, 2.0 and 4.0 were implanted into the lumbar muscle of rats for periods up to 18 months. Three rats were used for histological evaluation and three for breaking strength assessment at each survival time.

Very few rats survived beyond one year due to a pathological problem associated with the strain of rat used.

Tissue Reaction Assessment

Tissue reactions were described qualitatively and assessed quantitatively using a manually operated picture analyser. Tissue reaction areas from 1 to 120 days were between 0.11 and 0.42 mm^2 indicating an extremely low grade reaction which was unchanged at the longest period tested - 18 months.

Tensile Strength Assessment

Straight pull tests using an Instron tester were carried out on the explanted samples. PROLENE was shown to be very resistant to loss of tensile strength at all periods tested.

Study of Tissue Reaction to Colourless and Pigmented Polypropylene Sutures in the Ocular Tissues of the Rabbit

(Ethicon Inc Final Report, 14.10.65)

Summary and Conclusions

The reaction to size 5/0 colourless and pigmented sutures in tissue of rabbit eye was investigated in two series of experiments. In one group of 29 albino rabbits straight segments of sutures were placed in the palpebral conjunctiva. Four rabbits from this group were killed at 3, 5, 7, 10, 30 and 60 days after implantation. Histological evaluations were made of 11 sites implanted with colourless sutures and 17 sites implanted with pigmented sutures. In the second experiment sutures were evaluated in the rectus dorsal muscle and palpebral conjunctiva of 20 rabbits. Animals were killed after periods of 3, 7, 30 and 60 days, histological evaluations were made of 32 sites implanted with colourless sutures and 32 sites implanted with pigmented sutures.

Suture implants caused no appreciable damage to host tissues, the most characteristic reaction being a slight chronic inflammation. The implants retained their original characteristics and appeared to be completely inert.

VI.2. C A R C I N O G E N I C I T Y S T U D I E S

- Report of study by ETHICON Limited, 10/14/65

51

06021

Two Year Study of Tissue Reaction to Colourless and Pigmented Monofilament Polypropylene Sutures in the Dog

(Ethicon Inc Final Report, 14.10.65)

Summary and Conclusions

The biological behaviour of colourless and copper phthalocyanine blue pigmented polypropylene sutures was determined in four dogs in a two year study. Sutures, size 5/0 and 2/0, were implanted in the latissimus dorsi muscle as straight segments, continuous looping stitches, and as interrupted stitches. One dog was killed for histological evaluation of implant site after three months; the remaining three dogs after two years.

On gross examination the severed ends of the implanted segments appeared intact; no untoward reactions were noted.

Microscopically the sutures appeared as translucent, colourless or blue circles or ovals with regular outlines; neither phagocytosis of the implants nor dissolution were observed. Small fragments of polypropylene were seen in the vicinity of a few implants, both colourless and pigmented. These probably shredded off when knots were tied.

The reaction to the suture in most of the sites was slight and consisted of fibrous capsules infiltrated with varying numbers of macrophages. A somewhat larger number of macrophages and lymphocytes was seen in four implants, two colourless and two pigmented sutures. Since part of each of these implants was sutured into both muscle and fascia the increased reaction was probably caused by adhering tissues pulling on the sutures during movements of the animals. The type of reaction to colourless and pigmented sutures was similar as was the reaction after three months and after two years.

No neoplastic changes were observed.

Colourless and pigmented monofilament polypropylene sutures were well tolerated by dog tissue, caused a slight foreign body reaction, were not carcinogenic and were not absorbed within 24 months.

06022

Two Year Study of Tissue Reaction to Colourless and Pigmented Monofilament Polypropylene Sutures in the Rat

(Ethicon Inc Final Report, 14.10.65)

Summary and Conclusions

Colourless and phthalocyanine blue pigmented polypropylene sutures, sizes 2/0 and 5/0 were implanted into muscles and subcutis of 199 Sprague-Dawley rats. Rats were killed at intervals over a period of 24 months; implants and tissues were evaluated grossly and microscopically.

The reaction to colourless or pigmented suture in 45 rats maintained on test for 18 months or more was minimal, characteristic of a relatively non-irritating foreign body. The implants were surrounded by thin fibrous capsules whose interphase was infiltrated with few macrophages and fibroblasts. Several capsules hyalinised; giant cells were rarely seen. Reaction to both types of sutures after two years did not differ from that observed at one year. Microscopically, neoplastic changes in proximity of any suture were not observed, and all implants appeared intact grossly and microscopically.

On the basis of the experiment it was concluded that both colourless and pigmented polypropylene sutures were well tolerated by rat tissues, caused minimal foreign body reaction, were not carcinogenic, and were not absorbed during the 24 months test period.

VII. BIBLIOGRAPHY

VII.1. ABDOMINAL WALL

(SELECTION)

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Indications for selected operating methods in the treatment of post-operative eventrations of the antero-lateral abdominal wall. Proposals based on a series of 326 cases

by

R. Stoppa, X. Henry, J.P. Canarelli, S. Largueche, P. Verhaeghe, D. Abet and R. Ratsivalaka (*)

(*) Research from the Surgical Clinic of the UHC of Amiens.

Summary

The authors describe recent advances in operative procedures, which are related to the anatomy of the lesion, the physiopathological effects of severe eventrations, and the changes occurring in the lesion. This information can be used to improve analysis of individual prognosis, to improve patient preparation, to better evaluate the risk of possible failure of operative treatment, and for considering that wide prostheses with peritoneal reinforcement are the most satisfactory ones.

A critical study is made of the technical solutions available: raphes, true plastic procedures, autotransplants, and prostheses. The authors consider that among the prostheses, their choice would be one with peritoneal reinforcement with dacron tulle inserted without fixation (biological glue can be of interest here) into one deep divisible site of the parietal layers. The risk of sepsis can be avoided, or it must be treated, while conserving the prosthesis. Three methods are suggested as being valid: raphes for eventrations without "loss of substance"--"buried skin flaps in situ" for the most hazardous conjectures--inserted prostheses for the routine treatment of large eventrations.

A chart summarizing these opinions is presented, showing operative indications as a function of the site and extent of the eventration and its complications (sepsis, strangulation, relapse), and a multicenter study is suggested in order to make further advances in this direction.

The numerous failures, although difficult to quantify, that burden the surgical treatment of major post-operative eventrations should cause surgeons to have a spirit of inquiry with respect to this "iatrogenic" pathology which concerns them very specifically. At present, the recent factors capable of causing a reasoned development of tactics and techniques are the possibility of better analysing the circumstances and their physiopathological consequences, of preparing the patients better, and of better assessing the risks of failure in the traditional procedures, and finally of using selected procedures among which the large prostheses for peritoneal reinforcement occupy an important place.

We shall attempt here to give a critical tactical statement capable of enhancing the value of certain techniques at the expense of the traditional confidence accorded to others. Our experience has led us to adopt a chart of the indications of a reduced number of techniques judged to be reliable. It is this planning and these reflections that we are submitting for your appraisal.

I. The factors that should inspire the surgical tactics

I.1. The anatomy of the lesion

I.1.1. In practice, the eventration lesion is defined by its location, of course, but above all by the evaluation of a certain number of anatomical facts which when taken into account define the concept of "loss of parietal substance" (LPS) which implicates the difficulties of repair using the structures found at the site. Major eventrations, with a neck of more than 10 cm, are all LPSs for which repair is in principle very uncertain. To us, a diameter of less than 5 cm corresponds to a minor eventration without LPS. Between 5 and 10 cm in diameter, some eventrations with a poor wall should be considered like the LPSs. In reality, it is difficult to assess clinically the exact dimensions of the neck of an eventration, in particular when staggered eventrations are involved or when a septic event intervening in the etiology has caused a secondary fibrous degeneration of the edges.

I.1.2. For J. Rives (10), the facts to be taken into consideration are, above all, in the case of median eventration: the recoil of the insertions of the large muscles and their atrophy, as shown by the histological and biological examinations (cf. also J.P. Arnaud (4)); the sagitalization of the rectus muscles and the enucleation of the abdominal contents, under the action of the contractions of the abdominal support musculature, a factor in the loss of the "domiciliary right."

Another important element in the anatomical picture is the *reducibility or non-reducibility of the content*, about which we shall speak later.

It is also necessary to emphasize the complexity of the lesions encountered *in multirecurring eventrations* which end up by being considered as beyond therapeutic resources, although the risk of strangulation remains. Is this not a reason to assess with care the risks of failure of the traditional repair procedures so as to choose the most reliable techniques to start with? Finally, we want to emphasize the *importance of the peritoneal infundibulum*, a central element in the lesion which the repair should suppress as a "radical" zone. It must be accepted that there is eventration each time the plane of the fascia transversalis is crossed by the visceral sac. We deduce from this that *the only "radical" therapeutic method is that which renders the visceral sac ideally inextensible*, whatever the condition of the wall. In our current conception, this ideal method is the enveloping of the peritoneal sac by a flexible and sturdy large-size prosthesis which prevents recurrence (16).

I.1.3. All in all, *the typical eventration*, the problem eventration, is a major sub-umbilical median eventration because of its disastrous physio-pathological consequences and the practical difficulties of repairing it, resulting essentially from the loss of the "right to the city" of the "2nd abdomen" (Goni-Moreno) and the disproportion between the inadequacy of the remaining parietal structures and the dimensions of the breach to be repaired. *Eventrations* of the thoraco-abdominal, ilio-abdominal or lumbo-abdominal *borders* offer repair difficulties associated with the existence of a skimpy edge on which the attempts at reinsertion of the support musculature are tricky.

I.1.4. *In our own series of 326 post-operative eventrations* we have compiled 253 major eventrations (77%), 38 moderate eventrations (11.6%) and 35 minor eventrations (10.7%); with a total of 62 recurrent eventrations (19%).

I.2. Physio-pathological repercussions of major eventrations

The physiology of the abdominal wall is strongly associated with the mechanics of ventilation; this physiological interdependence between abdominal wall, diaphragm and thoracic cage has become as familiar to the surgeon as to the anesthesiologist-resuscitator. We give less thought to how much the abdominal wall participates, with the diaphragmatic pump, in the return circulation and, in opposition to the retrorachidic musculature, to the stato-kinetics of the trunk.

I.2.1. *Eventration: ventilation disorder*

The original concept of J. Rives on a respiratory eventration disorder (9) has the merit of inspiring our surgical indications and of giving a physiological purpose to our techniques. The LPS represented by the eventration brings about poor functioning of the diaphragm; at the level of the LPS itself, the wall, reduced to teguments, behaves like a shutter animated by paradoxical movements at the times of respiration. The respiratory eventration disorder is varied slightly by anatomical and clinical factors. The irreducibility of the content permits a "normal" functioning of the diaphragm by maintaining an intra-abdominal pressure before the operation, but implies a risk of ventilatory distress after surgical reduction of the content. Goni-Moreno has asserted since 1947 that the reduction of the content corresponds to the existence of an abdominal shutter, a factor for latent ventilatory insufficiency, liable to sudden decompensation due to low intra-abdominal pressure.

I.2.2. *Eventration: circulatory disorder*

This additional "tare" is shown in two ways, *systemic inferior vena cava stasis* due to inefficiency of the diaphragmatic pump and *splanchnic venous stasis* due to low intra-abdominal pressure. The consequences of this stasis are different in the pre- and post-operative phases. The post-operative thrombo-embolic risk is greater for major eventrations because of the associated respiratory disorder.

I.2.3. *Eventration: vascular disorder*

I.2.3.1. The parietal lesions of major median eventrations (muscular atrophy, sagittalization of the rectus muscles and recoil of the insertions of the lateral support musculature) can cause a *stato-dynamic defect* of the trunk, with lumbar lordosis, the significance of which depends on the inefficacy or the destruction of the anterior bracing by the "martingale" of the rectus muscles.

I.2.3.2. Inspired by various researches on *the electromyelographic study of the muscles of the antero-lateral wall of the abdomen*, with D. Abet (1) we tested the large rectus, large oblique and small oblique muscles with respect to 11 parietal areas in 100 patients with major eventrations. The results obtained can be classified quantitatively into 5 groups, according to whether the area is inactive (I), slightly active (II), moderately active (III), active (IV) or very active (V). Qualitatively, 5 areas seem to be the most interesting to explore, 1 and 10 corresponding to the large rectus, 4 and 9 to the large oblique and 11 to the small oblique muscles.

Taking into account the individual variability of the responses, and averaging the responses in the five main areas, we have available an overall criterion for the electromyelographic activity of the muscles of the abdominal support musculature. All together, the results, divided up into the five quantitative groups in the 100 cases tested, are as follows: 12 cases were classed in Group I, 20 cases in Group II, 48 cases in Group III, 12 cases in Group IV and 8 cases in Group V. There is no rigorous parallelism between the size of the eventration and the poor quality of the electromyelographic test but 80/100 major eventrations are found in Groups I, II or III. The future will tell if electromyelography of the muscular wall of the abdomen constitutes a practical criterion that it is indispensable to explore. We have personally derived from it the indication for a much more rigorous preparation of patients with major eventrations and a poor electromyelographic criterion.

I.2.3.3. *The trophic disease of the eventrated wall does not only affect the muscles;* the surgeon knows these atrophies well that reach all the planes, including the skin. Undoubtedly a recidivism factor is involved here after suturing or plastic surgery utilizing structures found at the site.

I.3. Evolutivity of the existing eventration

I.3.1. *The notion of speed of growth of the eventration*

This speed results from opposing factors, those that govern the expansion of the existing eventration and those that retard it. The most important factors here are obesity, parietal deterioration, the site of the eventration and the causes of high intra-abdominal tension (colopathy, exertion, etc.).

If it is difficult to predict the speed of growth for a given case, *it is possible to characterize this speed by considering groupings of cases.* For example, for a subject of average corpulence, epigastric eventration has a rate of growth higher than that of sub-umbilical eventration, but it stabilizes in 3 to 6 months whereas sub-umbilical eventrations with a large neck continue to grow regularly and for much longer. A thin subject with a poorly developed muscular wall makes eventrations that have a very slow rate of growth and relatively rapid stabilization, sometimes with a large neck but insignificant sac and bulging. Extreme evolutivities are represented by very tiny eventrations on one hand and by covered eviscerations on the other.

For us, taking the notion of speed of growth into consideration brings different therapeutic indications; we shall return to this.

I.3.2. *Evolutive problems*

We shall only cite those that, regardless of the operative risk, require a rapid or emergency surgical decision: *repeated obstruction* represents, besides again bringing into question the sometimes precarious equilibrium, a circumstance that stealthily aggravates the degenerative sclerosis of the parietal structures; *strangulation*, not always easy to confirm, endangering the vital prognosis and the early and prudent use of the pneumoperitoneum has been of service here in some cases by de-dramatizing a "tense" situation.

I.3.3. Preparation of the patient and the pneumoperitoneum (Goni-Moreno (18))

This involves *measures that are capable of influencing the evolutivity of an eventration* either because it is at a critical phase of its progress (obstruction, strangulation), or to improve the overall condition of a patient with a major eventration with a view to parietal repair.

We are completely convinced by the many works of Goni-Moreno that *the preparatory pneumoperitoneum should be part of the pre-operative conditioning* of major eventrations because not only does it improve the circumstances of the lesion, but it often also reduces the harmful consequences of major eventration on the ventilation and the sub-diaphragmatic venous circulation. In our series, we have used preparatory pneumoperitoneum 123 times in the group of 253 major eventrations (48.6%) with a very reduced number of minor incidents: scapular pain, 19 cases; parietal hematoma, 7 cases; parietal emphysema, 4 cases; retroperitoneal emphysema, 3 cases. The selection of the patients was made by the Goni-Moreno criteria (18). The average total amount insufflated was 10.5 l. The average duration of the preparation was 10 days with extremes of 4 days and 28 days.

Other contributions to the pre-operative preparation are a weight loss program and respiratory kinesitherapy; that is, a complex, sometimes long preparation is involved which can only be applied to its fullest extent in slow-growing eventrations.

1.4. Conclusions

I.4.1. A brief recall of the factors governing the technique of the surgical treatment of major eventrations, although combining factors of unequal importance, allows us to lay stress on: *the necessity of approaching the problem of the surgical treatment of eventrations in the spirit of clinical research that is indispensable* for the advent of the progress that remains to be achieved in the reliability of our parietal restorations; the usefulness of analysing *the components of the lesion and the long-term repercussions* so as on one hand to define the anatomical and physio-pathological objectives of the projected surgical operation, and on the other to assure the best pre-operative conditioning of the patients by appropriate preparation; and finally, to arrive at a universal classification of cases which would permit better evaluation of the observations and probably a better-founded choice of techniques depending on the precise evaluation of the hazards arising from the conditions.

I.4.2. In practice, it is now possible to put forward the following proposals:

a) *Major eventrations are not only "holes to be plugged"* but also a local and regional disorder affecting the mechanics of ventilation, sub-diaphragmatic venous circulation and spinal statokinetics.

b) *Their repair must call on differential indication procedures*: suturing and comparable procedures are only rarely possible or even desirable because of the consequences of the LPS; autoplasties using vicinal parietal structures are open to criticism because they add damage.

c) "Edge-to-edge" "patching together" with transplants or prostheses brings a partial solution of moderate solidity to the local problem and to the long-term physiopathological repercussions by reestablishing a relatively normal intra-abdominal pressure.

d) *Large prostheses to reinforce the peritoneal sac* are the most satisfactory whatever the dimensions of the LPS and the parietal degradation, at the same time as they normalize the respiratory, circulatory and statokinetic conditions.

II. Critical study of technical solutions

II.1. Suturing and derived procedures

II.1.1. We hardly ever use these well-known procedures using structures found at the site which are sutured without tension with non-absorbable thread. They include *extra-peritoneal procedures* (Quenu, d'Allaines and Contiades) and *intra-peritoneal procedures*, observing Condamin's principle (mattress suture of W. Mayo and Judd; procedure of Welti-Eudel).

It is possible to find some interest here in the "pulley" stitch which cuts less. Repair at several levels has less resistance to infection and traction "Support stitches" at a distance do not appear to bring additional security.

II.1.2. The standard indications for sutures and their derivatives are small and moderate eventrations such as partial eventrations after septic elimination of a wall suture thread and lateral eventrations in a drainage path. Overall, eventrations are involved that do not have true loss of substance from the abdominal wall and have a slow rate of growth. However, *these simple procedures cannot be considered to be satisfactory for major eventrations*. Undoubtedly, the current suture threads are of good quality, but the tissues brought together are cut if they are subjected to tractions that are too strong. Above all, as J. Rives (11) says, these procedures misjudge the physiopathology of major eventrations; they consist of reclosing the disunited wall like a first laparotomy is reclosed without taking into account the obvious setback and the lesions that appeared with the eventration, nor their physiopathological consequences.

It must also be said that *mistakes and abuses have been committed in the name of exclusive re-suturing*, such as large "mobilizing" dissections, the generous resection of the epiploon (rear wall of the oriento-parietal fissure), and above all the dangerously debilitating "discharge" incisions.

II.1.3. On the other hand, *a little piece of dacron gauze glued over the peritoneal sac* is an easily used means of reinforcement, capable of compensating and increasing the value of a re-suturing. We have used this without fail in operations for small eventrations for the last two years.

II.1.4. *In the series considered in this work, we used suturing or similar procedures 43 times* to treat: 28 small lateral eventrations, with 5 backup patches; 1 single recurrence out of 21 patients operated on and seen again after 6 months or more; 5 small median eventrations with two glued backup patches; no recurrence after 6 months or more; 10 moderate lateral eventrations, with 4 glued backup patches; 1 partial recurrence after 1 year.

II.2. True plastic surgery in situ

II.2.1. We refer here only to the procedures using parietal disinsertions, such as those of Sheerwood and Perelman (mobilizing the chondro-costal border), Daniel's myoplasties splitting the large rectus of the opposite side and Lanson's aponeurotic flaps. *These debilitating techniques do not seem advisable to us*, although we have no personal experience with them; they can perhaps be attempted in exceptional cases ("peripheral" eventrations).

II.2.2. *The criticisms that are applicable to all autoplasties in situ*, whether they are muscular or aponeurotic, are the following: the duration of the surgical procedure is often too long considering the hazards encountered; the use of structures deteriorated by the eventration, sometimes weakened still more by dissections or "mobilizations," is unsatisfactory and too high a tension resulting from the use of local structures risks the reproduction of the conditions that are at the origin of the eventration.

It thus seems that these procedures should only be considered under exceptional circumstances. Can they be "improved in value" by combining them with a piece of glued preperitoneal dacron gauze? We have no experience with this.

II.3. Autografts (autotransplantations)

II.3.1. We have no experience with aponeurotic (fascia lata) autografts in patches or strips. In the past we have employed the standard procedures using the skin rarely, and the skin lacing proposed by J. Gosset, then by Suire, Laflitte and Pavy, Juzbasic, Theodoresco, etc., not at all. Occasionally we have used *a total autogenous skin transplant* (Rehen, Mair, Green, then Pautet, Roux and Laurthe-Tolra, Judet, Morel-Fatio, Gautier-Benoit) (16) or a homogeneous one preserved with "Cialit." It must be remembered that total skin is an easily accessible source of fibrous tissue developed at the expense of the dermis, which can be buried with impunity, provided it is sutured like a "drumskin". Removal of the epidermis is then not useful. The reversal of the transplant seems preferable to facilitate phagocytosis of the epidermal debris in the peritoneal cavity as well as the revascularization of the transplanted dermis. It is useless and probably harmful to realize a complementary layer between the cutaneous transplant and the tegument, because the development of "epidermal cysts" is then a risk, a result of the wrinkling of the graft. The criticisms applicable to this technique are its length and the necessity of a large, sometimes very distant, removal from the abdominal field.

II.3.2. We would like to recall a procedure of our own, published in this journal with our professor J. Seror (12, 13), which we called the *cutaneous flap "buried in situ"* procedure. This combines the advantages of repairs using structures found at the site with those of plastic surgery, that is, simplicity and efficacy. A simple procedure, it is applicable to patients worried about recovery, but weary. As an extra-peritoneal procedure, it is better to reject it for eventrations with sub-occlusive problems; as a procedure assuring moderate security, the patient must be warned that he will sometimes be required to remain strapped up in a light corset.

II.3.3. In the series considered here, there are no skin patches. We had in the past used the "cutaneous flap buried in situ" procedure about thirty times with consistent results. A.A. Arianoff et al. have recently reported before the Belgian Society for Surgery on *a series of 71 cases* with 4 failures on 58 patients seen long-term (3).

II.3.4. Even if skin patches are a good answer to the physiopathological constraints of eventrations with major loss of substance and in particular in the conditions created by the eventration respiratory disorder, it is certain *that the reliability of the repair is moderate because of the defects inherent in the "patching up" that they achieve.* We think that skin patches should be strictly reserved for poor overall conditions both from the point of view of the general conditions and the local state, and in particular to eventrations with risk of infection, eventrations on an irradiated wall, in ascitic cirrhosis, or after covered evisceration (the rapid growth of these latter cases does not always permit a long enough reparation, especially for the pneumoperitoneum).

II.4. Prostheses

These have the advantage over grafts of avoiding the removal time and of being available in any dimensions; however it is only recently that they have become "good prostheses," dacron gauze being the best representative at present.

II.4.1. *Metal prostheses*

Metallic prostheses, in the form of silver wire, tantalum mesh (Burke 1940) and then steel wire (Thomeret 1960), were abandoned after the failures and accidents that are well known.

II.4.2. *Plastic prostheses*

These comprise a whole series of synthetic materials, the desirable qualities of which are strength, flexibility, permeability, and good tolerance (2, 7, 8), especially in septic environments, and the adherence to nearby tissues. It seems to us above all that *the "gauze" structure is among the most interesting* both to assure its light weight and good behavior in case of septic problems and also the *rapid autofixation* to the walls of the implantation fissure in the parietal layers. The animal experiments that we performed with J.Petit (7, 8) and our clinical experience (about 1000 parietal prostheses) are in agreement and have led us to be loyal to dacron gauze, which was proposed in France by J. Rives (11). We have never used the relatively pliable but impermeable patches of Rhodergon velvet (J. Gosset, Ph. Detrie (5)), or the non-pliable and non-permeable patches of siliconized material (Silastic). It may be recalled that prostheses had initially been used as superficial reinforcements of the suturing of the sheath of the rectus muscles, then after 1944 for the pre-peritoneal patching up of the loss of parietal substance, either at the deep face of the muscles, in front of the sutured peritoneal plane (Usher, Stock, Acquaviva), or in front of the posterior layer of the sheath of the rectus muscles (J. Rives (10, 11)), or on the superficial face of the rectus muscles (Chester Barclay) with more risks of infection. Around 1955, Usher, Bourgeon advocated their use intraperitoneally in direct contact with the viscera.

II.4.3. *This type of solution theoretically resolves the two main therapeutic problems (9):*

- The mechanical problem: to compensate for the insufficient parietal structures;

- The physio-pathological problem: to restore a moderate abdominal pressure in order to treat the ventilatory disorder by reestablishing the conditions of normal diaphragmatic functioning.

However, the prosthesis introduces a septic risk which is accompanied by constraints which we will discuss again. On the other hand, *"edge-to-edge" patching up subjects the sutures to tensions that can be high and the source of failure.*

II.4.4. Personally, we also propose *a much more reliable method, adaptable to all LPSs: the large reinforcement prosthesis for the peritoneal sac* which renders the latter non-extensible and prevents recurrence; we have used this for 8 years.

These are the principles of this method:

a) We chose *the Dacron gauze prosthesis* for the reasons previously discussed. Its good tolerance permits the use of very large-sized prostheses (30 cm x 30 cm) all the more so since the type of insertion desired is deep.

b) The choice of the implantation site of the parietal prosthesis is made between *four "good," "natural," deep sites in the "laminations" of the abdominal wall*: the inferior retro-parietal pre-peritoneal cleavable space (Retzius and Bogros), utilizable for median sub-umbilical eventrations; the sub-umbilical retro-parietal pre-peritoneal space, a little cramped, for median sub-umbilical eventrations; the sub-umbilical retromuscular space, in front of the posterior layer of the sheath, which can be used in median and para-median umbilical and sub-umbilical eventrations; finally, the intra-peritoneal "omento-parietal fissure," which can be used in umbilical and sub-umbilical median eventrations (15).

In our opinion, there are two sites of choice, the plane of the retro-parietal and inferior pre-peritoneal cleavage (used 155 times in our series) and the anterior cleavage plane of the posterior layer of the sheath of the rectus muscles (used 31 times in the series under consideration). Two others are used less frequently, the omento-parietal fissure and the sub-umbilical pre-peritoneal retro-parietal space (used 18 and 16 times, respectively). However, it is very often indispensable to carry out *"mixed" implantations* (6), by making 2 or more "natural" cleavage fissures communicate by dissecting so as to obtain a very wide peritoneal reinforcement (103 times in our series).

It is thought that the facility of cleavage of these sub-parietal spaces is reduced by successive re-operations. To us, this is one more reason to assess with appropriate seriousness the risk of failure of a traditional cure and to choose from the outset the procedure which best opposes recidivism.

c) The large sizes of the prostheses used contrasts them with "patches" (for parietal "patching") and permits their *insertion without direct fixation* to the edges of the loss of wall substance; they "hold" by face to face adherence in the parietal cleavage fissure, at first like a "tire patch" between inner tube and tire, secondarily by penetration of the granular tissue then inclusion in the scar fibrosis. It is possible to improve the immediate and early secondary stability of the prosthesis either by reconstituting if possible a more or less resistant superficial plane or by extending beneath it a small number of traction sutures transfixing the whole of the wall peripherally and fastened on "bolsters," or, finally, by using a biological cement sparingly (cf. below).

d) *The advantages of insertion without fixation* of the prosthesis into the parietal layers relative to "edge-to-edge" patching seem to us to be the reinforcement of the only plane that counts in the most radical concern possible, that for the peritoneal sac, and the non-fixation of the prosthesis which avoids failures due to the points of parietal necrosis due to pulling the fixation threads tight in the standard patching up.

e) *The use of a biological cement* is an initiative that we have practiced for a little more than two years. The animal experiments that we carried out with D. Abet (1), confirmed by our clinical practice (32 cases), caused us to choose the N-butyl-cyano-acrylate monomer used by neurosurgeons for many years. We use it by pointwise applications to replace the fixation stitches; the "glued" patch mechanically resists tangential traction just as well as when it is fixed by non-transfixing suture stitches. In certain cases it is possible not only to avoid any direct fixation (source of tightening necrosis), but even any indirect temporary fixation using threads fastened on bolsters (relatively delicate to maintain and causing exposure to infection from the skin).

II.4.5. *Infectious setbacks associated with the use of prostheses* must be discussed. We observe these in about 3% of cases out of several hundreds of operations, that is a rate comparable to that of "sepsis" after hernia treatment without prosthesis. These unpleasant setbacks represent a hazard similar to that of all surgery using a foreign material (orthopedics, cardiovascular surgery, etc.).

We think, with J. Rives (10), that this number can be reduced by taking technical precautions that are very accessible to the general surgeon: suitable operating room ("prosthesis room" or operation programmed "first" after careful disinfection of the room, laminar air flow?), "draping" the operating field, "no-touch technique," local per-operative antiseptic, close

post-operative monitoring. It must be said that the treatment of a septic setback does not imply the removal of the prosthesis even in case of severe infection. The infection must only be rigorously treated by drainage or irrigation-drainage of the suppurated collections, excision of fistular paths, in sum, by meticulous surgery adapted to the infection involved. Under these conditions, septic setbacks almost always heal by localized action preserving the dacron gauze prosthesis. Unfortunately, it is not the same for the "impermeable" prostheses made of Silastic or Rhodergon. It is certainly difficult to completely suppress setbacks associated with the use of prostheses, and the surgeon is confronted by the choice to be made between the septic risk and the risk of recidivism in some cases.

II.4.6. Finally, the indication for repair in the elderly must be weighed because these are long operations, especially when they have to be combined with another surgical procedure, for example at the same time resecting an excess cutaneous fatty apron, usefully, in a large obese woman prepared by a weight-loss treatment (14, 15).

II.4.7. In the series of 326 eventrations considered here, in *287 cases we used a large dacron gauze prosthesis reinforcing the peritoneal sac*, under the following circumstances: 253 major eventrations (221 median and 19 lateral) and also the 4 repeats that we observed in this group; 28 moderate eventrations (8 lateral and 20 median) as well as one repeat observed in the group operated on by suturing; finally, the repeat median minor eventration mentioned in the group operated on by suturing. We emphasize that 62 recurrent eventrations were all treated with a prosthesis. Here very briefly are the principal results of the 287 large prostheses: 2 early deceases in aged patients due to cardiac insufficiency (a risk that is probably poorly appraised) and pulmonary embolism (verified on autopsy); 6 suppurations, of which only 1 required ablation of the patch in the 3rd month. Of 239 patients seen again, we found after 6 months: 7 recurrences of which 2 were on walls that had already suppurated; with the other 5, in whom the walls had not yet suppurated, partial recurrences were involved that appeared suddenly after traumatism or great effort in large obese patients, twice after repair of low lateral major eventration.

II.5. At the end of the critical account of the operative techniques for dealing with eventrations, we ourselves shall stay with *three valuable and ordinary methods*:

- suturing and similar procedures (possibly protected by a glued dacron gauze patch), simple techniques that can be used for minor eventrations without loss of parietal substance, with no respiratory disorder;
- skin patches, for which it must be admitted that their resistance is good in septic or dystrophic environments, that they can be appropriate for large losses of substance, but that they give mediocre solidity and finally that when the terrain is deteriorating, it would be better to have recourse to *our own "cutaneous flap buried in situ" procedure;*
- *dacron gauze prostheses* inserted (without direct fixation to the edges - not as patches) into a fissure of the parietal cleavage (one of the deep sites defined above) so as to obtain a wide reinforcement of the peritoneal sac; this method is very reliable, but costly in operating time and blemished by the septic risk associated with the inclusion of prostheses. The use of biological cement seems to us to simplify the immediate fixation of the prosthesis and to promise consistent results.

We will mention only for the sake of completeness the *useful contributions* represented by post-operative corseting, kinesitherapy and cautious getting out of bed post-operatively.

III. Selective indications

III.1. These come from taking into account the etiological factors and the factor governing the risk of recidivism. We recall the main elements to be taken into consideration:

- *site*: lateral eventrations [are] less evolutive than median ones, especially the sub-umbilical median one (problem eventration); peripheral eventrations offer particular difficulties;
- *dimensions of the true loss of substance*, contrasting small eventrations (without loss of substance) and major eventrations (loss of substance of more than 10 cm in diameter) which make suturing alone hazardous;
- *state of the muscular wall*: to be explored clinically and perhaps by electromyelography; "good" walls have no atrophy and "bad" ones have muscular atrophy;
- *ventilatory after-effects*, to be evaluated without fail and to be corrected in very large eventrations by preparation of the patient;
- the *rate of growth*, resulting from the preceding elements, defining the evolutivity of the parietal lesions, a basic notion that is not always easy to assess individually;
- the *possibility of a rigorous preparation adapted* to the individual state of the patient, which is also valid as a prognostic test;
- everything *that governs the septic risk* and which can preclude the use of prostheses;
- finally, *the terrain*, with the following as the main aggravating elements: age, obesity, high intra-abdominal pressure factors, deteriorating defenses.

III.2. The anatomical and clinical polymorphism of eventrations requires being flexible and agreeing that no single technique permits the resolution of all the problems posed by the repair of major eventrations. However, it is also necessary to be "pessimistic" in the assessment of the risks of recidivism; in other words, even if many eventrations seem "restorable," it must not be forgotten that they will be more efficaciously treated with a prosthesis (Ph. Detrie (5)).

III.2.1. *Lateral eventrations*

a) *Small and moderate eventrations*, with a good wall, ordinarily have low evolutivity and minor ventilatory aftereffects; the typical case is the scar of an old, drained appendectomy. Here, suturing is legitimate and reliable, with the extra contribution of a retroparietal patch cemented on to the peritoneal sac for security in the more problematic cases.

b) *Major eventrations* have a muscular wall that is of poor quality and associated with a fairly rapid evolutivity. The exclusion of the content of the sac moderates the respiratory contribution for the lowest ones; the typical case is the eventration of a scar from a lumbar sympathectomy or nephrectomy by the antero-lateral route. Here it would be better to use a large prosthesis supported underneath in front and glued in back on to the peritoneal sac.

III.2.2. *Median eventrations*

a) *Small ones* with a good wall, of negligible evolutivity except in large obese patients with moderate or negligible ventilatory aftereffects, are frequent and represented by "defects" limited by "loosening" of a suture stitch on the linea alba or by the umbilical hernia in the adult. Here a repair can be effected by mattress sutures protected with a retroparietal patch cemented on to the peritoneal sac;

b) *Diastasis of the rectus* or *small tiered and multiple eventrations* are quite often subjected to the Welti-Eudel procedure reinforced by a glued patch, but it must be stated that a large prosthesis is more reliable here in the least favorable circumstances;

c) *Major eventrations*, especially sub-umbilical ones and even more so sub- and superumbilical eventrations after xiphopubic laparotomies for aortic surgery, are very poorly tolerated because of their rapid growth on bad walls and because of the major ventilatory after-effects. They are the typical indication for the very large prosthesis, supported underneath, after careful preparation of the patient. But the cases with risk of sepsis can cause a skin patch to be considered; the "poor risks" in a generally dangerous context can make the use of a cutaneous flap buried in situ obligatory.

III.2.3. *Eventrations with peripheral topography*

These are the ones that are located in the confines of the thorax and abdomen (after thoraco-phrenolaparotomy, after epicardial implantation of a pacemaker electrode, more rarely after subcostal incision); very near the iliac crest and in the thoraco-lumbar region.

Generally large in size, these LPSs can be repaired by means of *large prostheses supported underneath* by suture threads fastened on to bolsters transfixing the wall very far from the muscular edges and fixed with spots of cement under the rigid edges (chondrocostal rim or costal insertions of the diaphragm on top, fascia iliaca below). The placement of the L.P.P.R. [large prosthesis for peritoneal reinforcement] by the indirect route is strongly advised here.

III.2.4. *Complicated eventrations*

a) We will not stress the unfavorable circumstances represented by eventrations *on an infected or irradiated wall*, or on an ascitic abdomen. Let us say only that here we have had decent results after skin patching. Nonetheless, the realization of septic actions in the abdominal cavity as a rule contraindicates the use of a prosthesis even though we had some very pretty successes with prostheses put in place after intestinal resection or closure of a fistula of the small intestine in the same operating session.

b) Good surgical sense demands doing only what can be done on a wall with *strangulated eventration*. Resuturing alone is often practiced here, especially if an intestinal resection has been required, but in favorable cases we have been able to use a prosthesis.

c) *Finally, recurrent eventrations* must make consideration of a prosthesis imperative.

III.2.5. Overall, we willingly acknowledge that the field of indications for the standard means of parietal restoration has shrunk greatly in our practice, while that for very large prostheses for peritoneal reinforcement has expanded greatly. The limits of this last method are in no way determined by the extent of the parietal deterioration, but rather by the septic context on one hand and by general circumstances that are too bad on the other.

IV. Conclusion

What to do when confronted with post-operative eventration? We must recognize that this involves the consequences of the failure of the parietal closure and to analyse the causes of this; assess the evolutive risks of the LPS and its ventilatory and overall after-effects on the patient; evaluate the risks of failure of standard or minor techniques in accordance with a classification that we have tried to outline; prepare the patient rigorously

and appropriately. As far as the technical performance of the parietal repairis concerned: treat with care the "remaining" parietal structures and the large omentum, be restrictive in indications for suturing and autoplasty, have recourse to reasonable indications and without timidity to the large prostheses considered as a means of reinforcement of the peritoneal sac; and personally monitor the operative sequelae for 10 days, especially from the viewpoint of the risk of sepsis.

More practically, the question of "what to do" should be extended to the standard questions: "When?" and "How?". The answers to these questions represent primarily a range of proposals which extend from abstention from surgery (of which we have said little - due to non-indication or contraindication) to emergency surgery on a strangulated eventration. The importance of the rigorous preparation of the patient, and the taking into consideration of the long-term after effects of the disorder, especially the ventilatory ones, must be forcefully emphasized. However, the most important terms of the discussion concern the imperative or relative indications and contraindications for large gauze prostheses, a modern method which best answers the anatomical, clinical and pathophysiological requirements. We have attempted to justify our confidence, matched with constraints with respect to these prostheses, hoping that a multicenter experience will allow new advances in the future.

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Discussion

M. Garbay: I congratulate Stoppa for the quality of his results and above all for the small number of occurrences of sepsis and recidivism.

I think, however, that the sub-peritoneal placement of the patch imposes significant decollements, which can increase the risk of sepsis. I also believe that it is very important to "retighten" the large muscles to correct the physiopathological disorders noted by the author. The abdominal support musculature must find a support point to improve the vertebral statics and the respiratory problems.

Finally, as far as the importance of the pneumoperitoneum advocated by my Professor, Goni-Moreno, is concerned, I would like to recall how much he emphasized the "contracture" of the flanks as evidence of the retraction of the abdominal support musculature, since this tension should disappear when the succession of insufflations has permitted sufficient dilation of the abdominal cavity.

C. Houdard: Mr. Stoppa's communication has highlighted the physiopathology of large eventrations and, in particular, the part played by the disinsertion of the large muscles which take on a sagittal orientation.

Like the speaker, I believe in the essential value of a large prosthesis lining the peritoneal cavity, but it seems important to me to give the muscles their support point. As a consequence of the loss of parietal substance, the aponeurotic suture is not possible under excessive tension. The muscles must thus be given their function by a 2nd Tergal patch, sutured to the edges of the breach. The placement of a 2nd layer of inert material does not seem to have increased the morbidity of the technique.

Ph. Monod-Broca: I congratulate Stoppa on his excellent paper and the results he reports. I am only sorry that he did not formally distinguish between super-umbilical and sub-umbilical eventrations. For the latter, a prosthesis can almost always be avoided in favor of musculo-aponeurotic plastic surgery. Even so, the risk of sepsis is less for the latter technique.

Reprinted from ANNALS OF SURGERY, May 1981
Vol. 193, No. 5

07014

Management of Acute Full-thickness Losses of the Abdominal Wall

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Over a 20-year interval, 167 patients sustained acute full-thickness abdominal wall loss due to necrotizing infection (124 patients), destructive trauma (32 patients), or en bloc tumor excision (11 patients). Polymicrobial infection or contamination was present in all but five of the patients. Of 13 patients managed by debridement and primary closure under tension, abdominal wall dehiscence occured in each. Only two patients survived, the 11 deaths being caused by wound sepsis, evisceration, and/or bowel fistula. Debridement and gauze packing of a small defect was used in 15 patients; the single death resulted from recurrence of infectious gangrene. Pedicled flap closure, with or without a fascial prosthesis beneath, led to survival in nine of the 12 patients so-treated; yet flap necrosis from infection was a significant complication in seven patients who survived. The majority of patients (124) were managed by debridements, insertions of a fascial prostheses (prolene in 101 patients, marlex in 23 patients), and alternate day dressing changes, until the wound could be closed by skin grafts placed directly on granulations over the mesh or the bowel itself after the mesh had been removed. Sepsis and/or intestinal fistulas accounted for 25 of the 27 deaths. Major principles to evolve from this experience were: 1) insertion of a synthetic prosthesis to bridge any sizable defect in abdominal wall rather than closure under tension or via a primarily mobilized flap; 2) use of end bowel stomas rather than exteriorized loops or primary anastomoses in the face of active infection, significant contamination, and/or massive contusion; and 3) delay in final reconstruction until all intestinal vents and fistulas have been closed by prior operation.

ONE OF THE MOST PERPLEXING situations ever to confront the general surgeon is an open abdomen in the absence of adequate somatic substance to effect secure closure of the peritoneal cavity.[4,8,16] An obsession with the necessity to obtain fascia to fascia approximation, regardless of the tension, has appeared to be the overriding determinant of what action is taken to gain such an end. If, on the other hand, the surgeon attempts to obviate undue tension on the suture line, his debridement of contused and inflamed tissues becomes all too conservative for the massiveness of associated bacterial contamination. In either event, the outcome is uniformly predictable. There is the rapid onset of a necrotizing wound infection, which in turn serves as the initiating focus of a progressive, fulminating, and often lethal, more generalized, sepsis.

A modest experience in the management of patients with acute full-thickness defects of the abdominal wall has led to the identification of certain surgical tenets. Unfortunately, failure, especially if repetitive after a specific method of repair, has been much more instructive than has any success. In addition, correction or control of associated injuries and disease states may, in final analysis, hold the balance between eventual life and death.

The following is a retrospective review of these patients, as cared for on the Surgical Service of Grady Memorial Hospital.

Patient Review

During the 20 year interval from 1960 through 1979, 167 patients had major abdominal wall defects created by external violence, necrotizing soft tissue sepsis, or en bloc excision of primary or secondary neoplasia. The average age of the patients was 44.6 years, with a range of 3 to 84 years. There were 118 males and 49 females, 106 black patients and 61 white patients.

These large somatic defects were the result of radical debridement in 124 patients with necrotizing soft tissue sepsis, destructive abdominal wall trauma in 32 patients, or a sizable full-thickness gap consequent to wide en bloc tumor excision in 11 patients (Table 1). Associated disease states reflected an impairment in host defense function, such as diabetes mellitus and renal disease, or extremes in nutrition (Table 2). Prior laparotomies had been performed either for repair of transperitoneal hollow viscus injuries in 58 patients or

Presented at the Annual Meeting of the Southern Surgical Association, December 8–10, 1980, The Breakers, Palm Beach, Florida.
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Submitted for publication: December 11, 1980.

07015

TABLE 1. *Cause for Abdominal Wall Loss*

	Number of Patients	Died	Mortality Rate (Per Cent)
Necrotizing infection	124	31	25
Traumatic wound	32	12	38
En Bloc tumor excision	11	2	18
Total cases *	167	45	27

TABLE 3. *Bacteriology of Necrotizing Infections*

	Number of Patients	Died	Mortality Rat (Per Cent)
Streptococcal	4	1	25
Gas gangrene	7	4	57
Meleney's synergy	1	—	—
Noma	1	—	—
Polymicrobial synergy	111	26	23
Total patients	124	31	25

for corrections of intra-abdominal alimentary tract inflammatory processes in 46 patients.

Necrotizing Infection

Necrotizing infection of the abdominal wall was caused by a polymicrobial synergism between aerobic gram-negative rods and various anaerobic species in 111 patients (Table 3). Meleney's cellulitis and noma accounted for one symbiotic infection each. Classic gas gangrene occurred in seven patients, while pure aerobic streptococcal erysipelas led to extensive tissue necrosis in the remaining four patients.

The severity of the sepsis was reflected by the fact that 83, or 67%, of the 124 patients had an associated bacteremia (Table 4). Aerobic gram-negative rods, various anaerobes, and Enterococcus were the pathogens almost exclusively isolated from the blood. Clostridial bacteremia was attended by the highest mortality rate of any, *i.e.*, 54%.

Closure of the abdominal defect by approximation of debrided wound edges in two patients fostered a recurrence of sepsis, which then progressed on to fatal septicemia (Table 5). In two other patients, septic death resulted similarly from use of a pedicled abdominal flap. However, when the defect was relatively small, as in eight patients, and could be bridged by a gauze pack, persisting sepsis and eventual death followed in only one so managed. In 112 patients, larger defects not lending themselves to closure by a gauze plug were handled by insertion of a piece of synthetic mesh. Wound sepsis recurred and required at least one additional major debridement in 34 patients, (30%). Death followed in 24 patients (21%) as a result of such persisting sepsis with or without an associated small bowel fistula.

Overall, there were 29 deaths due to progressive wound sepsis, fulminating peritonitis, and/or bowel fistula, thereby producing a mortality rate of 23% on the basis of wound complications alone (Table 5). Two patients died of unrelated causes.

Destructive Trauma

Close-range shotgun blasts were responsible for 21 of the 32 abdominal wall losses caused by trauma (Table 6). An impalement accounted for five abdominal wall losses, while high velocity missiles and guillotine-like injuries, inflicted by railroad boxcar wheels, created three each. The majority of these patients (29 or 91%) presented with a penetrating wound of the abdomen. Other clinical findings included obvious evisceration, hemorrhagic shock in 22 patients, impalement in five patients, and traumatic hemipelvectomy in three patients.

An average of 3.3 associated organ injuries were noted in 31 of the 32 patients (Table 7). Gastrointestinal wounds were present in 30 of these 31 patients, and accounted for many of the postoperative septic complications. However, the greater amount of initial operative effort was directed toward control of the 13 associated major vascular injuries.

TABLE 2. *Associated Disease States in 124 Patients*

Associated Disease	Number of Patients
Diabetes mellitus	61
Cardiovascular disease	43
Renal insufficiency	33
Advanced liver disease	21
Obesity	46
Malnutrition	17
Prior operation for trauma	58
Prior operation for gastrointestinal disease	46
Miscellaneous disease states	81

TABLE 4. *Bacteremia/Septicemia in 83 of 124 Patients*

	Number of Patients	Died	Mortality Rate (Per Cent)
Gram-negative rods	69	24	35
Clostridia	13	7	54
Other anaerobes	63	17	27
Enterococcus	32	7	22
Other streptococci	9	2	22
Staphylococcus aureus	5	1	20
Total patients	83	29	35